

IN THE CLAIMS:

Kindly amend the claims as follows:

1 1. (Currently Amended) A method of detecting a
2 malignant tumor in a human subject, comprising:

3 (a) collecting a sample of a bodily substance containing human
4 nucleic acid or protein, said nucleic acid or protein having
5 originated from cells of the human subject;

6 (b) detecting quantitatively or semi-quantitatively in the sample
7 a level of expression for laminin α 4 subunit protein or
8 *laminin α 4-specific mRNA* complementary to a nucleic acid
9 of SEQ ID NO:1; and

10 (c) comparing the expression level in (b) to a level of
11 expression in a normal control, wherein overexpression of
12 laminin α 4 subunit protein or laminin α 4-specific mRNA,
13 with respect to the control, indicates the presence of a
14 malignant tumor in the human subject.

1 2. (Previously Presented) The method of Claim 1, wherein
2 the bodily substance is blood, urine, lymph, cerebro-spinal fluid, skin, stroma,
3 vascular epithelium, oral epithelium, vaginal epithelium, cervical epithelium,
4 uterine epithelium, intestinal epithelium, bronchial epithelium, esophageal
5 epithelium, or mesothelium.

1 3. (Previously Presented) The method of Claim 1, wherein
2 the bodily substance is a tissue sample.

1 4. (Original) The method of Claim 3, wherein the tissue
2 sample is collected from the brain of the subject.

1 5. (Original) The method of Claim 3, wherein the tissue
2 sample is a tumor tissue.

1 6. (Original) The method of Claim 1, wherein the bodily
2 substance is plasma.

1 7. (Original) The method of Claim 1, wherein the bodily
2 substance is a cellular material.

1 8. (Original) The method of Claim 7, wherein the cellular
2 material is derived from the human subject's brain kidney, bladder, ureter,
3 urethra, thyroid, parotid gland, submaxillary gland, sublingual gland, lymph
4 node, bone, cartilage, lung, mediastinum, breast, uterus, ovary, testis,
5 prostate, cervix uteri, endometrium, pancreas, liver, spleen, adrenal,
6 esophagus, stomach, or intestine.

1 9. (Previously Presented) The method of Claim 7, wherein
2 the cellular material is a carcinoma, sarcoma, lymphoma, mesothelioma,
3 melanoma, glioma, neuroblastoma, glioblastoma, oligodendroglioma,
4 astrocytoma, ependymoma, primitive neuroectodermal tumor, atypical
5 meningioma, malignant meningioma, or neuroblastoma.

1 10. (Previously Presented) The method of Claim 8, wherein
2 the cellular material is a hyperplastic and/or cytologically dysplastic cellular
3 growth or proliferation that is benign prostatic hyperplasia/dysplasia or cervical
4 hyperplasia/dysplasia.

11-12 (Cancelled)

1 13. (Previously Presented) The method of Claim 2, wherein
2 the expression level of *laminin* $\alpha 4$ -specific mRNA is detected by measuring
3 RNA.

1 14. (Currently Amended) The method of Claim 2, wherein
2 the expression level of *laminin* $\alpha 4$ -specific mRNA is detected by measuring
3 cDNA.

1 15. (Previously Presented) The method of Claim 2, wherein a
2 gene expression microarray is used to detect the level of expression of *laminin*
3 $\alpha 4$ -specific mRNA.

1 16. (Previously Presented) The method of Claim 1, further
2 comprising detecting the overexpression of laminin $\beta 1$ subunit protein or
3 *laminin* $\beta 1$ -specific mRNA relative to the normal control.

1 17. (Original Claim) The method of Claim 1, further
2 comprising detecting quantitatively or semi-quantitatively in the sample a level
3 of expression with respect to a normal control, of a gene encoding a protein
4 selected from the group consisting of insulin-like growth factor binding protein
5 precursor 3, transforming growth factor- β -induced gene, vascular endothelial
6 growth factor, connective tissue growth factor, human insulin-like growth
7 factor binding protein precursor 5, placental growth factor, transcription factor
8 Ap-2, human insulin-like growth factor II, epidermal growth factor receptor,
9 matrix metalloproteinase-2, keratin 18, vimentin, fibronectin 1, phospholipase
10 A2 receptor, desmoplakin, tropomodulin, tenascin C, and collagen type IV $\alpha 1$
11 chain, or detecting a combination of expression levels for any of these.

1 18. (Currently Amended) A method of diagnosing the
2 presence of a glioma in a human subject, comprising:

- 3 (a) obtaining a sample from the brain of the human subject;
4 (b) detecting quantitatively or semi-quantitatively in the sample
5 a level of expression for laminin α 4 subunit protein or
6 *laminin α 4-specific mRNA* complementary to a nucleic acid
7 of SEQ ID NO:1; and
8 (c) comparing the expression level in (b) to a level of
9 expression in a normal control, wherein overexpression of
10 laminin α 4 subunit protein or *laminin α 4-specific mRNA*,
11 with respect to the control, indicates the presence of
12 glioma in the subject.

19-20 (Cancelled).

1 21. (Previously Presented) The method of Claim 18, wherein
2 the expression level of *laminin α 4-specific mRNA* is detected by measuring
3 RNA.

1 22. (Previously Presented) The method of Claim 18, wherein
2 the expression level of *laminin* $\alpha 4$ -specific mRNA is detected by measuring
3 cDNA.

1 23. (Previously Presented) The method of Claim 18 wherein
2 a gene expression microarray is used to detect the level of expression of
3 *laminin* $\alpha 4$ -specific mRNA.

1 24. (Previously Presented) The method of Claim 18, further
2 comprising detecting the overexpression of laminin $\beta 1$ subunit protein or
3 *laminin* $\beta 1$ -specific mRNA relative to the normal control.

1 25. (Original Claim) The method of Claim 18, further
2 comprising detecting quantitatively or semi-quantitatively in the sample a level
3 of expression with respect to a normal control, of a gene encoding a protein
4 selected from the group consisting of insulin-like growth factor binding protein
5 precursor 3, transforming growth factor- β -induced gene, vascular endothelial
6 growth factor, connective tissue growth factor, human insulin-like growth
7 factor binding protein precursor 5, placental growth factor, transcription factor
8 Ap-2, human insulin-like growth factor II, epidermal growth factor receptor,
9 matrix metalloproteinase-2, keratin 18, vimentin, fibronectin 1, phospholipase
10 A2 receptor, desmoplakin, tropomodulin, tenascin C, and collagen type IV $\alpha 1$
11 chain, or detecting a combination of expression levels for any of these.

1 26. (Original Claim) The method of Claim 18, wherein the
2 sample is a tumor tissue.

1 27. (Original Claim) The method of Claim 18, wherein the sample
2 comprises plasma.

1 28. (Currently Amended) A method of predicting the
2 recurrence of a malignant tumor in a human subject from whom a tumor has
3 been resected, comprising:

4 (a) obtaining a tissue sample from the human subject, said tissue
5 sample being from a region adjacent to the site of the
6 tumor;

7 (b) detecting quantitatively or semi-quantitatively a level of
8 expression for laminin $\alpha 4$ subunit protein or *laminin $\alpha 4$ -*
9 *specific* mRNA complementary to a nucleic acid of SEQ ID
10 NO:1 in the sample; and

11 (c) comparing the expression level in (b) to a level of expression in
12 a normal tissue control, wherein overexpression of laminin
13 $\alpha 4$ subunit protein or *laminin $\alpha 4$ -specific* mRNA, with
14 respect to the control, is predictive of a recurrence of a
15 malignant tumor in the subject.

1 29. (Original Claim) The method of Claim 28, wherein the
2 tissue sample is histopathologically normal in appearance.

30 -31 (Cancelled).

1 32. (Previously Presented) The method of Claim 28, wherein
2 the expression level of *laminin $\alpha 4$ -specific* mRNA is detected by measuring
3 RNA.

1 33. (Previously Presented) The method of Claim 28, wherein
2 the expression level of *laminin* $\alpha 4$ -specific mRNA is detected by measuring
3 cDNA.

1 34. (Previously Presented) The method of Claim 28, wherein
2 a gene expression microarray is used to detect the level of expression of
3 *laminin* $\alpha 4$ -specific mRNA.

1 35. (Original Claim) The method of Claim 28, further
2 comprising detecting quantitatively or semi-quantitatively in the sample a level
3 of expression with respect to a normal tissue control, of a gene encoding a
4 protein selected from the group consisting of insulin-like growth factor binding
5 protein precursor 3, transforming growth factor- β -induced gene, vascular
6 endothelial growth factor, connective tissue growth factor, human insulin-like
7 growth factor binding protein precursor 5, placental growth factor,
8 transcription factor Ap-2, human insulin-like growth factor II, epidermal growth
9 factor receptor, matrix metalloproteinase-2, keratin 18, vimentin, fibronectin 1,
10 phospholipase A2 receptor, desmoplakin, tropomodulin, tenascin C, and
11 collagen type IV $\alpha 1$ chain, or detecting a combination of expression levels for
12 any of these.

1 36. (Previously Presented) The method of Claim 28, further
2 comprising detecting the overexpression of laminin $\beta 1$ subunit protein or
3 *laminin* $\beta 1$ -specific mRNA relative to the normal tissue control.

37-43 (Cancelled).

1 44. (Currently Amended) A method of predicting the
2 recurrence of a glioma in a human subject from whom a glioma has been
3 resected, comprising:

4 (a) obtaining a tissue sample from the brain of the human
5 subject, said tissue sample being from a region adjacent to
6 the site of the glioma;

7 (b) detecting quantitatively or semi-quantitatively a level of
8 expression for laminin $\alpha 4$ subunit protein or *laminin $\alpha 4$ -*
9 *specific mRNA* complementary to a nucleic acid of SEQ ID
10 NO:1 in the sample; and

11 (c) comparing the expression level in (b) to a level of expression in
12 a normal tissue control, wherein overexpression of laminin
13 $\alpha 4$ subunit protein or *laminin $\alpha 4$ -specific mRNA*, with
14 respect to the control, is predictive of a recurrence of
15 glioma in the subject.

1 45. (Original Claim) The method of Claim 44, wherein the
2 tissue sample is histopathologically normal in appearance.

46-47 (Cancelled).

1 48. (Previously Presented) The method of Claim 44, wherein
2 the expression level of *laminin $\alpha 4$ -specific mRNA* is detected by measuring
3 RNA.

1 49. (Previously Presented) The method of Claim 44, wherein
2 the expression level of *laminin* $\alpha 4$ -specific mRNA is detected by measuring
3 cDNA.

1 50. (Previously Presented) The method of Claim 44, wherein
2 a gene expression microarray is used to detect the level of expression of
3 *laminin* $\alpha 4$ -specific mRNA.

1 51. (Original Claim) The method of Claim 44, further
2 comprising detecting quantitatively or semi-quantitatively in the sample a level
3 of expression with respect to a normal tissue control, of a gene encoding a
4 protein selected from the group consisting of insulin-like growth factor binding
5 protein precursor 3, transforming growth factor- β -induced gene, vascular
6 endothelial growth factor, connective tissue growth factor, human insulin-like
7 growth factor binding protein precursor 5, placental growth factor,
8 transcription factor Ap-2, human insulin-like growth factor II, epidermal growth
9 factor receptor, matrix metalloproteinase-2, keratin 18, vimentin, fibronectin 1,
10 phospholipase A2 receptor, desmoplakin, tropomodulin, tenascin C, and
11 collagen type IV $\alpha 1$ chain, or detecting a combination of expression levels for
12 any of these.

1 52. (Previously Presented) The method of Claim 44, further
2 comprising detecting the overexpression of laminin $\beta 1$ subunit protein or
3 *laminin* $\beta 1$ -specific mRNA relative to the normal tissue control.

53-59 (Cancelled).

1 60. (Currently Amended) A method of ranking a malignant
2 tumor in a human subject, wherein said ranking orders the tumors in terms of
3 ~~invasiveness and aggressiveness, comprising:~~

4 (a) obtaining a tissue sample from the human subject, said
5 sample comprising a cell expressing a plurality of mRNA
6 species that are detectably distinct from one another;

7 (b) detecting quantitatively or semi-quantitatively an expression
8 level ~~for at least two of the plurality of mRNA species,~~
9 ~~wherein at least one of the detected mRNA species is a of~~
10 laminin α 4 subunit protein or laminin α 4-specific mRNA
11 complementary to a nucleic acid of SEQ ID NO:1 and at
12 ~~least one is specific to a growth factor-related gene or to a~~
13 ~~structural gene other than a laminin gene;~~

14 (c) constructing an expression profile of the sample comprising
15 a combination of the detected expression levels of *laminin*
16 *α 4*-specific mRNA and ~~the at least one other mRNA species~~
17 ~~specific to the growth factor-related gene or to the~~
18 ~~structural gene other than a laminin gene; and~~

19 (d) comparing the expression profile in (c) to an expression
20 profile for a normal tissue control, wherein a level of
21 overexpression of *laminin α 4*-specific mRNA, with respect
22 to the control, is indicative of the presence of and degree
23 of invasiveness of the tumor in the subject, ~~wherein a level~~
24 ~~of overexpression of the structural gene other than a~~
25 ~~laminin gene, with respect to the control, is indicative of~~
26 ~~degree of tumor invasiveness, and wherein a level of~~
27 ~~overexpression of the growth factor-related gene, with~~
28 ~~respect to the control, is indicative of degree of tumor~~

29 aggressiveness.

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1 61. (Currently Amended) The method of Claim 60, further
2 comprising a step of detecting an expression level of and a step of comparing
3 said expression level of at least one growth factor-related gene or a structural
4 gene other than a laminin gene or products of said genes wherein the growth
5 factor-related gene encodes a protein selected from the group consisting of
6 insulin-like growth factor binding protein precursor 3, transforming growth
7 factor- β -induced gene, vascular endothelial growth factor, connective tissue
8 growth factor, human insulin-like growth factor binding protein precursor 5,
9 placental growth factor, transcription factor Ap-2, human insulin-like growth
10 factor II, and epidermal growth factor receptor.

1 62. (Currently Amended) The method of Claim ~~60~~ 61,
2 wherein the structural gene encodes a protein selected from the group
3 consisting of matrix metalloproteinase-2, keratin 18, vimentin, fibronectin 1,
4 phospholipase A2 receptor, desmoplakin, tropomodulin, tenascin C, and
5 collagen type IV α 1 chain.

1 63. (Original Claim) The method of Claim 60, wherein the
2 expression level of *laminin α 4*-specific mRNA is detected by measuring RNA.

1 64. (Original Claim) The method of Claim 60, wherein the
2 expression level of *laminin α 4*-specific mRNA is detected by measuring cDNA.

1 65. (Original Claim) The method of Claim 60, wherein a
2 gene expression microarray is used to detect the level of expression of *laminin*
3 $\alpha 4$ -specific mRNA.

1 66. (Original Claim) The method of Claim 60, further
2 comprising detecting the overexpression of *laminin* $\beta 1$ -specific mRNA relative
3 to the normal tissue control.

1 67. (Original Claim) The method of Claim 60, wherein the
2 tissue sample is brain tissue.

1 68. (Original Claim) The method of Claim 60, wherein the
2 tumor is a glial tumor.

69-74 (Cancelled).

1 75. (Previously Presented) The new method of Claim 1,
2 further comprising detecting the overexpression of a gene encoding laminin $\beta 1$
3 subunit relative to the normal control.

1 76. (Previously Presented) The method of Claim 18, further
2 comprising detecting the overexpression of a gene encoding laminin β 1 subunit
3 relative to the normal control.

1 77. (Previously Presented) The method of Claim 28, further
2 comprising detecting the overexpression of a gene encoding laminin β 1 subunit
3 relative to the normal control.

1 78. (Previously Presented) The method of Claim 44, further
2 comprising detecting the overexpression of a gene encoding laminin β 1 subunit
3 relative to the normal control.